



Acoustic Tweezing Cytometry Induces Rapid Initiation of Human Embryonic Stem Cell Differentiation and Accelerate Neural Tube-Like Rosette Formation

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Abstract:

Mechanical forces play critical roles in influencing human embryonic stem cell (hESC) fate. However, it remains largely uncharacterized how local mechanical forces influence hESC behavior in vitro and the impact of dynamic mechanical forces on neural induction of hESCs. Here, we used an ultrasound (US) technique, acoustic tweezing cytometry (ATC), to apply targeted cyclic subcellular forces to hESCs via integrin-bound microbubbles (MBs). We found that ATC-mediated cyclic forces applied for 30 min to hESCs near the edge of a colony induced immediate global responses throughout the colony, suggesting the importance of cell-cell connection in the mechano-responsiveness of hESCs to ATC-applied forces. ATC application generated increased contractile force, enhanced calcium activity, as well as decreased expression of pluripotency transcription factors Oct4 and Nanog, leading to rapid initiation of hESC differentiation and characteristic epithelial-mesenchymal transition (EMT) events that depend on focal adhesion kinase (FAK) activation and cytoskeleton (CSK) tension. Further, Accelerated neural induction of hESCs is demonstrated as the result of combined action of ATC and neural induction medium (NIM). Specifically, application of ATC for 30 min followed by culture in NIM upregulates neuroectoderm markers Pax6 and Sox1 as early as 6 h after ATC, and induces neural tubelike rosette formation at 48 h after ATC. In contrast, no changes are observed in hESCs cultured in NIM without ATC treatment.

These results reveal a unique, rapid mechano-responsiveness and community behavior of hESCs to integrin-targeted cyclic forces.



Biography:

- Results-driven, analytical biomedical engineer with 8+ years of experience in tissue engineering, microfluidics, biomaterials, and molecular biology techniques.
- Prolific researcher as evidenced by 11 fellowships and 5 awards, totaling \$450,000+ of support; 5 publications, 1 book chapter, 30+ talks and presentations
- Leadership experience developed through student mentoring and training, serving as a graduate student instructor, and leading a student organization at the University of Michigan

Publication of speakers:

- Colman A, Dreesen O. Pluripotent stem cells and disease modeling. *Cell Stem Cell*. 2009;5:244-247. doi: 10.1016/j.stem.2009.08.010. [PubMed]
- Pouton CW, Haynes JM. Embryonic stem cells as a source of models for drug discovery. *Nat Rev Drug Discov*. 2007;6:605-616. doi: 10.1038/nrd2194. [PubMed]

[International Webinar on Tissue Engineering and Regenerative Medicine; November 23, 2020; Singapore city, Singapore](#)

Citation: Tugba Topal; Acoustic Tweezing Cytometry Induces Rapid Initiation of Human Embryonic Stem Cell Differentiation and Accelerate Neural Tube-Like Rosette Formation; International Webinar on Tissue Engineering and Regenerative Medicine; November 23, 2020; Singapore city, Singapore.